

THE REMARKS

The Amendments

Claim 1 is amended to include the limitation of Claim 6, and Claim 6 is canceled.

No new matter is added in any of the above amendment and the Examiner is respectfully requested to enter the amendments and reconsider the application.

The Response

Claims 1-9 are pending.

1. Objection to drawings

The drawings were objected to for informalities. Applicants are hereby submitting a new set of drawings addressing the issues.

2. 35 U.S.C. §103(a) rejections

Claims 1-9 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shimada, *et al.* (WO 96/29349) and Wistuba, *et al.* (Journal of Virology, Sept. 1995) and further in view of Harlow (Antibodies, a laboratory manual, 1988). The rejection is traversed in parts and overcome in parts in view of the amendments.

Harlow, *et al.*, disclose strategies for testing elution conditions for immunoaffinity purification. At page 551, the reference states that "there are no good shortcuts nor any guaranteed useful buffers. The best strategy is to test small antibodies in elution conditions as possible."

The reference also discloses: "If trying for the gentlest elution conditions, start with acid conditions first, then check basic elution buffers. If these conditions do not elute the antigen, try others. A general order to check the various conditions would be: acid, pH 3-1.5; base pH 10-12.5; MgCl₂, 3-5 M; LiCl 5-10 M; water; ethylene glycol 25-50%; dioxane 5-20%, thiocyanate 1-5 M; guanidine 2-5 M; urea 2-8 M; SDS 0.5% to 2%." (Page 551)

Harlow, *et al.* disclose a general strategy for immunoaffinity purification. Each pair of antigen and antibody has unique features in terms of activity and stability, which affect the design

of a purification protocol. Until reduction to practice, it is not known if any one of the conditions that Harlow, *et al.* disclose would work for a specific antigen/antibody pair. There is no suggestion in Harlow, *et al.*, as to how to purify and concentrate AAV-2. Not all the conditions that Harlow, *et al.* disclose are suitable for elution of AAV-2 from antibody-linked chromatographic materials. Based on Harlow, *et al.*, a person skilled in the art would not have know to use an elution condition of 2-3 M MgCl_2 for elution AAV-2.

The advantage of the present invention is that the immobilized antibody is not denatured or separated from the column during the elution of AAV-2 by 2-3 M MgCl_2 , but continues to be bonded to the column, so that the column can be used several times after its regeneration. Furthermore, the purified viruses remain stable and infectious in the elution buffer of 2-3 M MgCl_2 . Example 2 and Figures 2 and 3 have illustrated that using 2.5 M MgCl_2 as an elution solution, a complete recovery of AAV-2 was achieved; and the virus remained infectious.

Shimada, *et al.*, disclose a monoclonal antibody specifically recognizing adeno-associated virus CAP protein. The specific monoclonal antibody can be used for the detection of an adeno-associated virus and the purification of adeno-associated virus vectors for gene therapy. The reference does not teach or suggest an elution condition of 2-3 M MgCl_2 , which is the feature of the present invention. Further, the reference does not teach an antibody specific to AAV-2.

Wistuba, *et al.*, disclose the immuno precipitation of Rep proteins by antibody A20. The reference does not teach or suggest an elution condition of 2-3 M MgCl_2 .

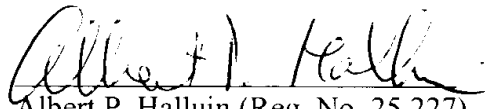
Applicants respectfully submit that the Examiner is not allowed to use hindsight construction using Applicants' invention as a blueprint to pick and choose different elements from different references to produce the claimed invention.

Therefore, the 35 U.S.C. §103(a) rejection of Claims 1-9 should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, the Applicants believe the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 463-8109. A telephone conference is especially requested if the Examiner intends to maintain the present rejections.

Respectfully submitted,



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